ABSTRACT

Antinociceptive Effect of Chloroform Extract and Ethanol Fraction of *Piper retrofractum* Vahl. Fruit in Mice: Involvement of COX-2 Inhibition Mechanism

Analgesic compounds are widely used throughout the world but can cause some adverse effects. This issue encourages studies to find alternative medicine derived from plants. *P.retrofractum* extract has an analgesic effect on mice, but there is no further information on its antinociceptive mechanisms. One of the most widely used tests to determine the antinociceptive effect is nociception induction by injecting formalin in plantar areas of experimental animals. Intraplantar injection of formalin causes recurrent syndrome of apparent nociceptive behavior in two distinct phases.

In the present study, the effect of chloroform extract and ethanol 96% fraction of *P.retrofractum* fruit on spontaneous pain behaviors and expression of COX-2 were examined in mice. The method used is the induction of pain using formalin injected at the plantar area of the hind paw of the mouse. Furthermore, an immunohistochemical examination was performed to validate the expression of COX-2.

Based on the one-way ANOVA statistical analysis followed by Tukey test, there was a significant difference in the decrease of mice pain response and foot edema between treatment group of chloroform extract and ethanol fraction with negative control group ($p < 0,05$). It appears that at the same dose containing piperine, the expression of COX-2 in the ethanol fraction group was lower than that of the chloroform extract group. These results indicate that there are other compounds besides piperine that contained in *Piper retrofractum* which are also responsible for provide analgesic activity.

Keywords: *P. retrofractum*, Nociception, Formalin, COX-2, IHC